2:45

795-4 Environmental Tobacco Smoke Causes Endothelial Dysfunction That Is Prevented by L-Arginine in Normocholesterolemic Rabbits

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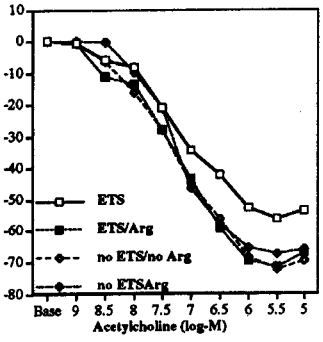
We have previously shown that chronic dietary arginine (Arg) supplementation with arginine prevents endothelial dysfunction in environmental tobacco smoke (ETS) exposed rabbits rendered hypercholesterolemic by diet. To examine whether Arg prevents endothelial dysfunction in normocholesterolemic rabbits exposed to ETS, the effects of Arg (2.25% solution ad libitum) and ETS (smoking chambers for 10 weeks) were studied in 32 rabbits fed a normal diet, in a 2 × 2 design. Acetylcholine, calcium ionophore A23187, and nitroglycerin-induced vasorelaxation were assessed in aortic rings precontracted with phenylephrine.

The results were analyzed with a general linear model ANOVA. ETS reduced endothelium-dependent acetylcholine-induced relaxation, and L-arginine blocked this adverse effect ($p = 0.04$). ETS tended to increase phenylephrine-induced contraction ($p = 0.06$). Neither ETS nor Arg influenced A23187-induced relaxation nor endothelium-independent nitroglycerin-induced relaxation.



Conclusion: 10 weeks of ETS causes endothelial dysfunction in normocholesterolemic rabbits without atherosclerosis, that is prevented by dietary supplementation with L-arginine.

3:00

795-5 Inducible Nitric Oxide Synthase Inhibition Reverses Impaired Arteriolar Responsiveness to Endothelin-1 in Sepsis

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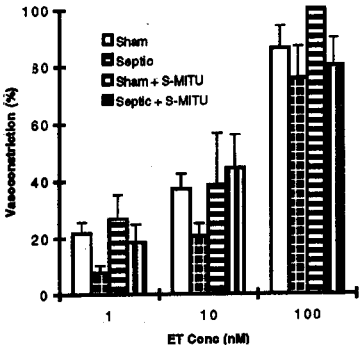
Introduction: Persistent vasodilation refractory to pressor agents is a characteristic hemodynamic abnormality in septic shock. Induction of nitric oxide synthase (NOS) by cytokines has been hypothesized to play a role in this refractory vasodilation. Using *in vivo* videomicroscopy, we examined the effects of topically applied endothelin-1 (ET-1) in septic and control rats.

Methods: Rats made septic by cecal ligation and puncture were compared to controls that underwent sham ligation. Using image-shearing videomicroscopy, maximal vasoconstriction in response to topically suffused ET-1 was measured in cremasteric resistance arterioles (15–20 microns) of septic and control rats. These measurements were taken before and after suffusion of the muscle with the selective inducible NOS (iNOS) inhibitor S-methyl-isothiourea (SMT).



Results: The microvasculature of septic rats was hyporesponsive compared to control rats. This abnormality was reversed by suffusion of the muscle with SMT (sham n = 13, septic n = 17; $p < 0.05$).

Conclusion: Impaired vasoconstriction in response to endothelin-1 in resistance arterioles of septic rats *in vivo* was reversed by selective iNOS inhibition. Previous studies have demonstrated the same response using the nonselective NOS inhibitor, N^G-methyl-L-arginine. This suggests an important role for nitric oxide in the refractory vasodilation seen in patients with septic shock.

3:15

795-6 Oral L-arginine Improves Endothelium-Dependent Dilatation and Reduces Monocyte Adhesion to Endothelial Cells in Young Men with Coronary Artery Disease

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Oral L-arginine (L-arg) improves endothelium-dependent dilatation (EDD), reduces monocyte/endothelial cell (M/EC) adhesion and decreases atheroma in cholesterol-fed rabbits. We therefore studied the effects of oral L-arg on EDD and M/EC adhesion in humans with known coronary artery disease (CAD).

In a prospective, double-blind, randomized crossover trial, 10 men aged 41 ± 2 years with CAD were studied after 3 days taking either oral L-arg (7 g tds) or placebo. Using ultrasound, brachial artery diameter was measured at rest, after flow increase (leading to EDD) and after sublingual nitroglycerin (an endothelium-independent dilator). The effect of each subject's serum on M/EC adhesion was measured in vitro. Serum collected after L-arg or placebo was added to human umbilical vein ECs and incubated for 24 hours. Human monocytes obtained by elutriation were then added to these ECs for 1 hour and M/EC adhesion assessed by light microscopy.

After oral L-arg, compared to placebo, EDD was improved (4.7 ± 1.1 vs 1.8 ± 0.7%, $p < 0.04$), M/EC adhesion was reduced (42 ± 2 vs 50 ± 1%, $p < 0.01$) and serum L-arg levels were increased (318 ± 18 vs 124 ± 9 μmol/l, $p < 0.01$). Reduction in M/EC adhesion could be reversed by in vitro addition of the arginine antagonist L-NMMA. No differences were seen in resting blood pressure, heart rate, fasting lipid levels nor in the vasodilator response to GTN.

In young men with CAD, oral L-arg improves endothelial function and reduces monocyte-endothelial cell adhesion. As in animal models, this may impact favorably on the atherogenic process.

796 Advances in Management of Hypertrophic Cardiomyopathy

Wednesday, March 19, 1997, 2:00 p.m.–3:30 p.m.
Anaheim Convention Center, Room C1

2:00

796-1 Pacing in Hypertrophic Obstructive Cardiomyopathy (PIC). A Randomised Crossover Study

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Dual chamber pacing (DDD) with short AV delay reduces left ventricular obstruction (LVOT grad) and relieves symptoms in patients with hypertrophic obstructive cardiomyopathy (HOCM), however, only reported from uncontrolled studies. In PIC 83 HOCM patients were randomised to three months each of active (DDD_{on}) or inactive (AAI30 = DDD_{off}) DDD pacing in a blinded crossover study.

Material and Methods: All patients had a resting LVOT grad ≥30 mm Hg, drug-refractory symptoms and were under consideration for myectomy. At baseline and after each study period LVOT grad, exercise tolerance (ETd), 24 h ECG, NYHA class and QoL were evaluated.

Results: Eighty-two patients completed the study protocol. Early reprogramming from DDD_{off} to DDD_{on} was requested by 17 patients, 14 of whom after entering the period on DDD_{off}, due to persistent or reoccurring symptoms. At the end of the study the DDD_{on} period was preferred by 90% of the patients. Two needed myectomy, while 80 continued on DDD-pacing. During DDD_{on} the LVOT grad was reduced from 59 ± 36 to 30 ± 25 ($p < 0.001$),